

=> s adenovirus and (E2F) (5A) promoter
L1 223 ADENOVIRUS AND (E2F) (5A) PROMOTER

=> s adenovirus and (E2F) (3A) promoter
L2 196 ADENOVIRUS AND (E2F) (3A) PROMOTER

=> s adenovirus and (E2F) (3A) promoter (S) (termination or insulator or polya or polyadenylation)
L3 2 ADENOVIRUS AND (E2F) (3A) PROMOTER (S) (TERMINATION OR INSULATOR
OR POLYA OR POLYADENYLATION)

=> d ibib abs 1-2

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:676177 CAPLUS

DOCUMENT NUMBER: 137:211937

TITLE: Construction of adenoviral vectors containing
insulating sequence for minimization of leaky
therapeutic gene expression

INVENTOR(S): Gorziglia, Mario; Hallenbeck, Paul L.; Kaleko,
Michael; Clarke, Lori; Phipps, Sandrina; Jakubczak,
John Leonard

PATENT ASSIGNEE(S): Novartis A.-G., Switz.

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002068627	A2	20020906	WO 2002-US5280	20020222
WO 2002068627	A3	20030612		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003104624	A1	20030605	US 2002-81961	20020222

PRIORITY APPLN. INFO.: US 2001-270885P P 20010223

AB The present invention relates to adenoviral vectors and their use in methods of gene therapy. The present invention provides novel viral vectors and methods useful for the minimization of leaky gene expression, and, in particular, of nonspecific transcriptional read-through of genes. Such constructs may be obtained by the insertion of an insulating sequence into a vector construct, such as for example a termination signal sequence upstream of the transcription initiation site of the resp. transcription unit. Provided is a recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a termination signal sequence, an E2F-1 promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR.

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:675779 CAPLUS

DOCUMENT NUMBER: 137:210924

TITLE: Oncolytic adenoviral vectors expressing therapeutic
genes for the treatment of cancer

INVENTOR(S): Ennist, David Leonard; Forry-Schaudies, Suzanne;
Gorziglia, Mario; Hallenbeck, Paul L.; Hay, Carl M.;
Jakubczak, John Leonard; Kaleko, Michael; Ryan,
Patricia Clara; Stewart, David A.; Xie, Yuefeng;
Connelly, Sheila; Police, Sehidhar Reddy; Clarke,
Lori; Phipps, Sandrina; Cheng, Cheng

PATENT ASSIGNEE(S): Novartis Pharma A.-G., Switz.

SOURCE: PCT Int. Appl., 226 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002067861 A2 20020906 WO 2002-US5300 20020222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003104625 A1 20030605 US 2002-81969 20020222

PRIORITY APPLN. INFO.:

US 2001-270922P P 20010223

US 2001-295037P P 20010601

US 2002-348670P P 20020114

AB The present invention relates to oncolytic adenoviral vectors and their use in methods of gene therapy. Provided is a recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR. The adenoviral vectors may also comprise a polynucleotide encoding a cytokine such as GM-CSF that can stimulate a systemic immune response against tumor cells. The preferred vector Ar6pAE2fF comprises an adenovirus vector that uses a fragment of the human E2F-1 promoter to selectively regulate E1A expression and thus adenoviral replication in tumor cells. Ar6pAE2fF selectively kills Rb-pathway defective tumor cells over normal primary cells, and is preferentially replicated in human tumor cell lines vs. normal primary cells. This vector has a superior early toxicity profile to the non-selective replication competent virus, Addl327, when administered i.v. in SCID mice and provides advantages in efficacy, selectivity, and safety as compared to the oncolytic viral vector Addl1520. Ar17pAE2fTrtex is a particularly preferred, tumor-selective oncolytic adenovirus designed for the treatment of a broad range of cancer indications involving the two most common alterations in human cancer, namely defects in the Rb-pathway and overexpression of telomerase. Ar17pAE2fTrtex utilizes a E2F-1 promoter to control expression of the adenoviral E1A gene and the adenoviral E4 gene is controlled by a hTERT (human telomerase reverse transcriptase) promoter. Ar17pAE2fTrtex is expected to replicate in the majority of cancer cells, lead to tumor selective expression of toxic viral proteins, cytolysis, and enhancement of sensitivity to chemotherapy, cytokines, and cytotoxic T lymphocytes.

FILE 'MEDLINE, CAPLUS' ENTERED AT 08:19:17 ON 03 SEP 2003

L1 6 S ITR (10A) (POLYADENYLATION OR POLYA OR POLY (A) ADENYLATION)
L2 4 S (HETEROLOGOUS OR CMV) (A) PROMOTER (10A) (POLYADENYLATION OR
L3 10 S (HETEROLOGOUS OR CMV) (A) PROMOTER (10A) (POLYADENYLATION OR
L4 6 S L3 NOT L2
L5 6 DUP REM L4 (0 DUPLICATES REMOVED)
L6 7 S ITR (5A) (TERMINATION OR POLYADENYLATION OR POLYA)
L7 6 S L6 NOT L4
L8 6 S L7 NOT L3
L9 5 DUP REM L8 (1 DUPLICATE REMOVED)